

### **REMARKS**

Claims 2-23 and 25-41 are pending in the present application. Claims 19, 20, and 34-41 are withdrawn. By virtue of this response, claim 5 has been amended. Accordingly, claims 2-18 and 21-23 and 25-33 are currently under consideration.

New rejections are levied under Section 112, paragraph 2 and Section 103. Applicant notes that claims 2 and 10-18 were allowed in the last Office Action (Paper No. 19), but presently stand rejected under Section 103. The Examiner did not state that the outstanding rejections of claims 1, 3-9 and 24 under Section 112, 2d paragraph (indefiniteness), claims 1, 3-9 and 24 under Section 112, first paragraph (written description), claims 21-33 under Section 112, first paragraph (enablement) and claims 1, 3-5 and 7 under Section 102, but did not re-levy these rejections. Thus, these rejections do not apply to the claims currently under examination before entry of this amendment.

With respect to all amendments and cancelled claims, Applicant has not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicant reserves the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional application. Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned “**Version with markings to show changes made**”.

### ***Information Disclosure Statements***

Applicant thanks the Examiner for reviewing and initialing the Form PTO-1449s.

### ***Drawing***

Applicant notes that formal drawings are submitted herewith. Applicant believes that the drawings address the comments in the draftperson's review.

### ***Objection to claim 9***

Applicant notes that the Office Action Summary states that claim 9 is objected to, but that the objection to claim 9 is not discussed in the body of the Office Action. Applicant respectfully requests clarification as to the nature of the objection to claim 9. Alternatively, withdrawal of this objection is solicited.

### ***Regarding claims 5 and 6***

Applicant thanks the Examiner for pointing out that claims 5 and 6 are not withdrawn from the present application. Review of the Office Action dated July 18, 2001 (Paper No. 15) confirms that these claims were not withdrawn from prosecution following Applicant's response to the earlier restriction requirement. Applicant notes that in the present response, claim 5 has been amended, and Applicant withdraws its request to rejoin claims 5 and 6.<sup>1</sup>

### ***Rejections under 35 U.S.C. § 112, second paragraph***

The Office has rejected claims 5, 11, 16, 26, and 31 as indefinite under 35 U.S.C. § 112, second paragraph, for allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

#### **Claim 5**

Claim 5 is rejected as allegedly indefinite on the ground that "it is unclear what applicant intends to claim in claim 5". See Office Action, page 2.

Applicant notes that claim 5 has been amended so that it depends only from claim 2. To the extent that the dependence from now-canceled claim 1 formed the basis of the Examiner's rejection, Applicant submits that this obvious typographical error is an improper ground for an

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<sup>1</sup> Applicant notes, however, that the Office Action dated March 27, 2001 (Paper No. 11) requested an election of species, and that in the Response dated May 2, 2001, Applicant elected the species recording alternations in protein expression. Should the Examiner decide to withdraw claims 5, and 6 at this time, based on Applicant's election of the species recording alternations in protein expression, Applicant respectfully resubmits its request to rejoin claims 5 and 6 upon allowance of a claim that encompasses the withdrawn species.

indefiniteness rejection. *See* "Advance notice of changes to MPEP §2173.02 clarifying Office policy with respect to rejections made under 35 U.S.C. Section 112, second paragraph," Memorandum from Stephen C. Kunin to the Patent Examining Corps., dated January 17, 2003 (*hereinafter*, "Advance notice of changes to MPEP §2173.02").

Applicant submits that this claim is clear. To the extent that some other ground is relied on in the rejection, Applicant requests clarification from the Examiner as to why "it is unclear what applicant intends to claim in claim 5". *See* Office Action, page 2; *see also* "Advance notice to MPEP §2173.02", *supra* at page 2, stating "an analysis as to why the phrase(s) used in the claim is "vague and indefinite" should be included in the Office action."). Withdrawal of this rejection is respectfully requested.

Claims 11, 16, 26 and 31

Claims 11 and 26 stand rejected as allegedly indefinite for reciting the phrase "therapeutic agent". The Examiner states that "it is unclear as to the metes and bounds of what would be considered "therapeutic agents?" and that "the specification fails to specifically define the phrase . . . ." Office Action, page 2. Claims 16 and 31 stand rejected as allegedly indefinite for reciting the phrase "animal therapeutics." The Examiner states that "it is unclear as to the metes and bounds of what would be considered "animal therapeutics?" and that "the specification fails to specifically define the phrase . . . ." Office Action, page 3. Applicant respectfully traverses these rejections.

As a preliminary matter, Applicant respectfully submit that this rejection is improper under the "Advance notice of changes to MPEP §2173.02", *supra*. Specifically, the Examiner has not provided "an analysis as to why the phrase(s) used in the claim is "vague and indefinite" should be included in the Office action." Instead, the Examiner merely states that "it is unclear as to the metes and bounds of what would be considered [animal therapeutics or therapeutic agents]" and that "the specification fails to specifically define the phrase[s] . . . ." (Office Action, page 2, 3), and does not provide any analysis as to why the offending phrases are allegedly indefinite. Accordingly, the rejection is improper and should be withdrawn.

Moreover, Applicant points out that the "Advance notice of changes to MPEP §2173.02" also states that if "modes of expression selected by applicant satisfies the statutory requirements of 35 U.S.C. § 112, second paragraph, but the examiner merely wants the applicant to improve the clarity or precision of the language used, the claim must not be rejected under 35 U.S.C. § 112, second paragraph, rather, the examiner should suggest improved language to the applicant." In the present Office Action, the Examiner did not make any such suggestions as to improved claim language.

Turning to the substance of the rejection, Applicant respectfully submits that the Examiner has applied an improper legal standard for this rejection. Specifically, the rejection is based (in part, if not in whole) on the ground that no definition is provided in the specification. However, neither the law nor the MPEP requires that claim terms be defined in the specification. Thus, prompt withdrawal of this rejection is respectfully requested.

Claims are definite where "the claims, read in light of the specification, reasonably apprise those skilled in the art and are as precise as the subject matter permits. As a matter of law, no court can demand more." Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1385, 231 USPQ 81, 94, 95 (Fed. Cir. 1986). Applicant respectfully submits that one of skill in the art understands the meaning of "therapeutic agent" and "animal therapeutic", as used in the present claims and specification. The specification defines "agent" at page 7, lines 22-27. Enclosed herewith is the Webster's Dictionary definition of "therapeutic" confirming the ordinary meaning of that term as "of or relating to the treatment of disease or disorders by remedial agents or methods" and "providing or assisting in a cure". The phrases also appear throughout the specification (see, e.g., at page 1, lines 30-36; page 3, line 32 to page, line 4; page 8, lines 22-25; page 14, line 303-32, and page 15, line 33 to page 16, line 11).

As a further example, Applicant notes that a search of the USPTO issued patent database reveals that 1347 issued patents use the phrase "therapeutic agent" in the claims, and 39 issued patents use the phrase "animal therapeutic" in the claims.

In summary, Applicant submits that one of ordinary skill abundantly understands the meaning of "therapeutic" and "animal therapeutic," and that use of these phrases is acceptable under the MPEP, the Office guidelines, and the law, and in view of the disclosed subject matter and the specification. Withdrawal of this rejection is respectfully requested.

#### **Rejections under 35 U.S.C. § 103(a)**

The Office has rejected claims 2-8, 10-18, 21-23, and 25-33 under 35 U.S.C. Section 103 as allegedly obvious over Spielmann et al., 1997 (In Vitro Toxicology, Vol. 10, No. 1, p. 119-127) in view of Craig et al., 1996 (Biomarkers, Vol. 1, No. 2, p. 123-135 and Wobus et al., 1999 (US Patent 6,007,993). According to the Office, "it would have been obvious for one of ordinary skill at the time of the invention to substitute the MTT cytotoxicity assay as taught by Spielmann with detection of gene expression as taught by Craig or detection of protein expression as taught by Wobus because it was known in the art to determine the effect of a chemical compound by detecting the alteration of gene expression or alteration of protein expression." Office Action, page 6.

Applicant respectfully traverses this rejection. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, the prior art reference(s) must teach or suggest all the claim limitations. Second, there must be some suggestion or motivation to modify the reference or to combine reference teachings. Third, there must be a reasonable expectation of success. *See* M.P.E.P. § 2143. The rejection of claimed subject matter as obvious in view of a combination of prior art reference requires consideration of whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, and whether the prior art would also have revealed that such persons would have reasonable success. Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the Applicant's disclosure. *See In re Vaeck*, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991).

Applicant respectfully submits that the Examiner has not made a *prima facie* case of obviousness because the Examiner has not shown that the cited references teach each and every limitation of the rejected claims. Moreover, the Examiner has not shown a suggestion or motivation to combine the Spielmann reference with the Wobus or Craig references, nor has the Examiner shown that there is a reasonable expectation of success. Applicant will address these points in turn.

The Examiner has not demonstrated that the cited references teach each and every limitation of the claims. The Office Action cites Spielmann as allegedly disclosing:

a method of using mouse embryonic stem cells *in vitro* for embryotoxicity testing comprising culturing the embryonic stem cells to a stage where the cells form embryoid bodies, contacting the bodies with a variety of chemical compositions, and determining the cytotoxicity of the chemical compositions by MTT cytotoxicity assay. Office Action, page 4. Spielmann uses 16 test chemicals which are assigned to three classes of *in vivo* embryotoxicity and compiles libraries of the "molecular profiles"<sup>2</sup> of the test chemicals and ranks the chemical compositions with respect to their relative toxicities.

Office Action, page 4 (citations omitted)

However, as noted in the Amendment filed December 18, 2001, Spielmann et al. use mouse embryonic stem cells, kept in an undifferentiated state, for the cytotoxicity screening assay. The Examiner cites pages 120 and 121 in the rejection, but these pages also describe use of undifferentiated embryonic stem cells in the MTT toxicity assay. See page 120, last paragraph through page 121, first paragraph (describing the ES cell cytotoxicity method). For example, page 120 describes cell culture conditions useful for maintenance of embryonic stem cells in the undifferentiated state by the addition of LIF. Pages 120-121 describe determination

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<sup>2</sup> Applicant disagrees that the MTT cytotoxicity test constitutes a "molecular profile", as suggested by the Examiner in the rejection. As noted in the Amendment filed December 18, 2001, the MTT cytotoxicity test is used to detect dead embryonic stem cells, and, indeed, Spielmann et al. merely counted the number of dead or alive embryonic stem cell colonies following exposure to the tested chemical compounds. Thus, it is evident that the MTT cytotoxicity test is not a method of detecting alterations in expression of sets of genes or proteins, as required by the present claims.

cytotoxicity with 3T3 cells and D3 ES cells. Indeed, even the abstract and the conclusion of Spielmann refer to an "EST," or embryonic stem cell test. See abstract; pages 125-126.

The Examiner also relies on Figure 1 of Spielmann in support of the present rejection. However, as noted in the previous Amendment, Figure 1 of Spielmann (on page 120) does not describe the method cited by the Examiner for determining the cytotoxicity of chemical compositions by measuring embryoid body cell death via the MTT cytotoxicity test. Rather, this figure describes Spielmann's cell differentiation assay, which is a completely different assay than the ES cell cytotoxicity assay cited in this rejection. As such, this figure is not pertinent to the grounds asserted in the Examiner's rejection.

Thus, the Spielmann cytotoxicity assay of embryonic stem cells does not involve "contacting a mammalian embryoid body" as required by the present claims, contrary to the grounds stated in the rejection. Craig and Wobus are cited as allegedly teaching "detection of gene expression" and detection of protein expression", respectively. Office Action, page 6. Accordingly, neither Wobus nor Craig remedy the limitations of Spielmann. Accordingly, the Examiner has not made a *prima facie* case, and withdrawal of this rejection is respectfully requested.

Applicant further submits that the Examiner has not shown a suggestion or motivation to combine the Spielmann reference with the Wobus or Craig references, nor has the Examiner shown that there is a reasonable expectation of success. The rejection of claimed subject matter as obvious in view of a combination of prior art reference requires consideration of whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, and whether the prior art would also have revealed that such persons would have reasonable success. Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the Applicant's disclosure. See *In re Vaeck*, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991). By contrast, in the present rejection, the Examiner merely states:

[i]t would have been obvious for one of ordinary skill at the time of the invention to substitute the MTT cytotoxicity assay as taught by Spielmann with detection of gene expression as taught by Craig or detection of protein expression as taught by Wobus because it was known in the art to determine the effect of a chemical compound by detecting the alteration of gene expression or alteration of protein expression."

and

[o]ne ordinary [sic] skill in the art at the time the invention was made would have been motivated to do so in order to generate a gene expression profile or protein expression profile of a teratogenic agent by using embryos or embryoid bodies . . . with reasonable expectation of success.

Office Action, page 6.

Thus, the Examiner points to the disclosure in Wobus and Craig of detection of gene expression or protein expression, and merely states that this disclosure would provide a suggestion or motivation to combine the Spielmann reference with the Wobus or Craig references, with a reasonable expectation of success. Applicant submits that this cursory discussion does not constitute an "convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teaching of the reference."

MPEP § 2142.

Moreover, Applicant notes that Spielmann reference states that "[t]he EST is ready to undergo validation in other laboratories" (abstract), and that "[t]he EST should be evaluated in other laboratories and more chemicals should be tested in the new test" (page 126). Thus, Spielmann itself notes that the results disclosed in the article are somewhat preliminary and should be "validated", "evaluated" and "tested" in other laboratories. One of ordinary skill, reading Spielmann, would be motivated merely to verify or validate the results disclosed in Spielmann, not to further modify Spielmann as suggested by the Examiner. Moreover, there is certainly no reasonable expectation of success in further modifying the test disclosed by Spielmann, when even the authors of Spielmann concede that the test they disclose must be "validated" and "evaluated" by others.

Thus, because of lack of motivation to combine as well as lack of reasonable expectation of success (either of which alone is sufficient to preclude obviousness), it is evident that a *prima facie* case of obviousness has not been made. Applicant respectfully requests withdrawal of this rejection.

For the record, Applicant notes that the Examiner did not state in the rejection that Spielmann, or Spielmann in combination with Wobus and Craig teaches the subject matter recited in the rejected dependent claims. For the record, Applicant notes that it has not been demonstrated that the cited references teach human embryoid bodies (claims 10, 25); chemical compositions with other than teratogenic toxicities (as required in claims 11, 16 and 31); chemical compositions as described in claims 13, 18, and 33; or methods of ranking toxicity (claim 23). Accordingly, a *prima facie* case of obviousness has not been made. Withdrawal of these rejections is respectfully requested.

## CONCLUSION


Applicant has, by way of the amendments and remarks presented herein, made a sincere effort to overcome rejections and address all issues that were raised in the outstanding Office Action. Accordingly, reconsideration and allowance of the pending claims are respectfully requested. If it is determined that a telephone conversation would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the unlikely event that the fee transmittal is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 441472000100. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: February 10, 2003

By:

  
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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**In the Claims:**

Please amend claim 5 without prejudice or disclaimer.

5. (Amended) The method of claim [1 or ]2, wherein the molecular profile comprises alterations in gene expression.